

What is claimed is:

1. A solution formulation comprising:
(a) a physiologically tolerated mixed buffer system comprising TRIS combined with a buffering molecule which:
(i) absorbs carbon dioxide; and
(ii) does not contain a free amine group; and
(b) a polypeptide.
2. The formulation of claim 1, wherein the polypeptide is prone to aggregation.
3. The formulation of claim 1, further comprising zinc, wherein the zinc forms a stabilizing complex with the polypeptide.
4. The formulation of claim 1, further comprising a phenolic preservative.
5. The formulation of claim 1, wherein the buffering molecule is selected from the group consisting of acetate, phosphate and citrate.
6. The formulation of claim 5, wherein the buffering molecule is phosphate.
7. The formulation of claim 4 further comprising an isotonicity agent.
8. The formulation of claim 7, wherein the polypeptide is insulin.
9. The formulation of claim 8, wherein the insulin is a monomeric insulin analog selected from the group consisting of LysB28ProB29-human insulin and AspB28 human insulin.
10. The formulation of claim 8, wherein TRIS is present at a concentration of about 1.5 mg/ml to about 4.5 mg/ml; phosphate is present at a concentration of about 0.2 mg/ml to about 2.5 mg/ml, insulin is present at a concentration of about 250 to about 1000 U/ml, zinc is present at a concentration of about .07 µg/ml to about .09 µg/ml, m-cresol is present at a concentration of about

2.2 mg/ml, phenol is present at a concentration of about 0.9 mg/ml and glycerol is the isotonicity agent and is present at a concentration of about 16 mg/ml.

11. The formulation of claim 10, wherein TRIS is present at a concentration of about 2 mg/ml to about 3 mg/ml and phosphate is present at a concentration of about 0.5 mg/ml to about 1.5 mg/ml.

12. The formulation of 8 for use in a continuous infusion system.

13. A method for treating diabetes comprising administering an effective dose of the formulation of claim 8 to a patient in need thereof.

14. A method for treating diabetes comprising administering an effective dose of the formulation of claim 8, wherein the formulation is administered using a continuous infusion system.

15. A method for treating hyperglycemia comprising administering an effective dose of the formulation of claim 8 to a patient in need thereof.

16. The method of claim 15, wherein the formulation is administered using a continuous infusion system.

17. A stable, soluble formulation of insulin for use in a continuous infusion system, comprising: an isotonicity agent; a mixed buffer system comprising TRIS combined with a buffer selected from the group consisting of phosphate buffer, acetate buffer and citrate buffer; insulin; zinc; and a phenolic preservative.

18. A process for preparing the monomeric insulin analog formulation of claim 9 comprising the steps of combining a physiologically-tolerated mixed buffer system comprising TRIS combined with a buffer selected from the group consisting of phosphate buffer, acetate buffer and citrate buffer; with the monomeric insulin analog; zinc; and a phenolic preservative.

19. A method of stabilizing a polypeptide prone to aggregation comprising combining the peptide with a physiologically-tolerated mixed buffer system comprising TRIS mixed with a buffering molecule that

does not contain a free amine group and which counteracts carbon dioxide; zinc; and a phenolic preservative.

20. The method of claim 19, wherein the buffering molecule is selected from the group consisting of acetate, phosphate and citrate.

21. The method of claim 19, wherein the mixed buffer system further comprises an isotonicity agent.

22. The method of claim 19, wherein the polypeptide is a monomeric insulin analog selected from the group consisting of LysB28ProB29-human insulin and AspB28 human insulin.

23. The method of claim 22, wherein TRIS is present at a concentration of about 1.5 mg/ml to about 4.5 mg/ml; phosphate is present at a concentration of about 0.2 mg/ml to about 2.5 mg/ml, the monomeric insulin analog is present at a concentration of about 250 to about 1000 U/ml, zinc is present at a concentration of about .07 µg/ml to about .09 µg/ml, m-cresol is present at a concentration of about 2.2 mg/ml, phenol is present at a concentration of about 0.9 mg/ml and glycerol is the isotonicity agent and is present at a concentration of about 16 mg/ml.

24. The method of claim 23, wherein TRIS is present at a concentration of about 2 mg/ml to about 3 mg/ml and phosphate is present at a concentration of about 0.5 mg/ml to about 1.5 mg/ml.